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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,954	03/19/2004	Marise S. Gottlieb		8077

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ROBERT E. BUSHNELL & LAW FIRM
2029 K STREET NW
SUITE 600
WASHINGTON, DC 20006-1004

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,954	GOTTLIEB, MARISE S.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-18 are pending in the application.

Claims 1-4, 6-18 have been rejoined, the restriction requirement issues on 9 May 2006 has been withdrawn because the claims as amended now present overlapping subject matter. Claims 1-4, 6-18 are presented for examination on the merits.

Any previous rejection, which is not further restated herein, is withdrawn.

Sequence Compliance

The application is now in sequence compliance (see specification amendment of 28 August 2008).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 6-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to several methods of treatment comprising Purified Leukocyte Dialysate Subfraction. With regards to the term “Purified Leukocyte Dialysate Subfraction”, the disclosure provides the following guidance: “The "selected immunoregulators" ("selected immunormodulators" "selected immunoamplifiers") include the purified Leukocyte

Dialysate Subfraction (LDS) described by Dr. A. Arthur Gottlieb Patents (U.S. Pat. Nos. 5,100,663, 4,616,079, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,321 which are incorporated herein by references) which is naturally derived from healthy human leukocytes, as well as purified immunologically active components of the naturally derived immunoregulators including the dipeptide tyrosylglycine (YG) and the tripeptide tyrosylglycylglycine (YGG), as well as synthetically produced YG and YGG. These regulators also include covalently modified YG and YGG, such modifications designed to stabilize or to enhance the biological activity of said regulators, as well as pharmaceutically acceptable salts, suitable for human use, of YG, YGG, and related molecules including covalently modified YG, and covalently modified YGG. " ([0041])." However, the disclosure is silent with regards to how to determine what is a subfraction in general (beyond the cited patents) and the term "Purified Leukocyte Dialysate Subfractions" encompassed a myriad of subfractions which are not expressly defined in a manner that shows possession of the full scope of the claimed subfractions. It would therefore require undue experimentation as applicant has not shown possession nor adequate guidance to obtain the full scope of purified leukocyte dialysate subfractions having the therapeutic activities as instantly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Gottlieb (EP 0230 052 A2).

Gottlieb teaches a method for preventing chronic inflammation due to the presence of or potential exposure to a pathogen, environmental particulates, or environmental toxins, said method comprising administering to said individual an effective dosage of a pharmaceutical composition selected from the group consisitng of YG-Product, YGG-Product, Purified Leukocyte Dialysate subfraction and a combination thereof (e.g., abstract, lines 6-14; claims 1-4, 18-24). Please note that preventing chronic inflammation does not require that the administered subject have any inflammation, nor does it required to be exposed to any pathogen, environmental particulates or environmental toxins. Therefore, the reference anticipates the instant claim above.

Claims 11-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gottlieb (EP 0230 052 A2) as evidenced by Brennan (Springer Semin Immunopathol, 1998).

Gottlieb teaches a method for mitigating a symptom in a patient, said symptom characteristic of chronic inflammation, said patient presenting said symptom, said method comprising administering to the patient a pharmaceutical preparation containing an effective dosage amount of YG-Product, YGG-Product, Purified Leukocyte Dialysate Subfraction, or a combination thereof. Gottlieb teaches administration of YG, YGG or derivatives thereof extracted from leukocyte dialysates derived from human white blood cells to treat immune deficiency imbalances such as that seen in rheumatoid arthritis

(e.g., abstract). The limitations of claims 12-13 and 15-16 "wherein said patient has at least one component of the Metabolic Syndrome" and wherein said component is "a proinflammatory state" necessarily read upon rheumatoid arthritis as evidenced by Brennan et al. The limitation of claim 17: “deferring the progression of a patient from the Metabolic Syndrome" reads also upon administration of YG, YGG or purified leukocyte dialysate subfraction to patients as taught by Gottlieb.

Therefore, the reference is deemed to anticipate the instant claims above.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Gottlieb (US 4,699,898).

Gottlieb teaches a method for preventing chronic inflammation (as in claim 10). Please note that the method does not require the patient to be affected with chronic inflammation. See Examples 6 and 7 which teach administering YGG to cancer and AIDS patients. Therefore the administration reads upon prevention of chronic inflammation.

Therefore, the reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb (EP 0230 052 A2) in view of Persselin (Clin Orthop Relat Res, 1991).

Gottlieb teaches a method for controlling rheumatoid arthritis in an individual, comprising administering to said individual an effective dosage of a pharmaceutical composition of YG-Product (e.g., abstract, lines 6-14; page 25, lines 22-29; page 45, lines 1-6). Gottlieb also teaches administering YG-Product with a dermal patch to treat a diabetic, which reads upon an individual having Metabolic Syndrome (see, e.g., page 45, lines 6). Gottlieb does not teach that rheumatoid arthritis is a chronic inflammation disease nor does it teach using elevated levels of C-Reactive Protein, serum fibrinogen, platelet count or platelet activity as markers for chronic inflammation.

Persselin teaches that rheumatoid arthritis necessarily reads upon a chronic systemic inflammatory disease (page 73, column 1, lines 1-3) and that elevated C-reactive protein levels (i.e., a proinflammatory state) and platelet counts serve as indicators of disease activity (e.g., abstract, lines 20-23).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Gottlieb by administering YG-product to a diabetic suffering rheumatoid arthritis using a dermal patch as taught by Gottlieb. Even if Gottlieb taught only diabetes type 1, the skilled in the art would have been motivated to combat diabetes type 2-related inflammation or environmentally generated chronic inflammation with YG-product, which was known to treat chronic inflammation (Gottlieb; page 25, lines 22-29, page 45, lines 1-6). There would have been a reasonable expectation of success, given that Gottlieb taught treating chronic inflammation in

rheumatoid arthritis patients and also taught use of a dermal patch administration of YG-product on diabetics (see, e.g., page 45) which was faster, required less skill and was less annoying to patients, plus it had a long lasting therapeutic effect. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-4 and 6-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb (US 4,699,898).

Gottlieb teaches treating a patient with cancer (Example 6, columns 10-11) with TGG (i.e., YGG product). Gottlieb also teach treating AIDS patients (Example 7) with TGG in order to improve their immune system. Although neither patient is identified as having the metabolic syndrome or symptoms thereof, it would have been obvious to one of ordinary skill in the art to apply YGG to patients of cancer and AIDS which would present at least one metabolic syndrome symptom (such as obesity, high blood pressure, hypercholesterolemia, etc) and having the metabolic syndrome. One of ordinary skill in the art would have been motivated to do so since there are no limitations expressly taught by Gottlieb with regards to the type of patient that would respond to the immune boosting to YGG product. Moreover, the limitations in the preamble “controlling inflammation”, “mitigating a symptom”, “preventing chronic inflammation”, and so forth, necessarily read upon the method of Gottlieb since it teaches the instant steps. The limitations of claim 18 are taught in Examples 6-7, which teach blood tests measuring the patient’s immune system, however, the Examples do not expressly teach monitoring inflammation and glucose level. The adjustment of

particular conventional working conditions (e.g., determining types of patients that respond to the treatment, determining appropriate health indicators within such method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., type of patients [e.g., having obesity, high blood pressure, metabolic syndrome, and so forth) and health parameters to be measured as health indicators], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions including type of patients wherein the method can be effective, in the safest and most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 8-16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8 and 13 of U.S. Patent No. 4,710,380. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to a method for controlling chronic inflammation (e.g., rheumatoid arthritis, claim 4 of US '380) in an individual comprising: administering to said individual an effective dosage of a pharmaceutical composition selected from the group consisting of YGG-Product (claim 13 of US '380). Please note that TGG and YGG are equivalent terms as stated above. The adjustment of particular conventional working conditions (e.g., determining types of patients that respond to the treatment within such method) is deemed merely a matter of judicious selection and

routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., type of patients to be applied to such as obese, with metabolic syndrome, and so forth], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions including type of patients wherein the method can be effective, in the safest and most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Further, the instantly claimed method encompasses and/or is encompassed by the claimed method of US '380.

Claims 1-4 and 6-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8 and 13 of U.S. Patent No. . 4,699,898.

Gottlieb teaches treating a patient with cancer (Example 6, columns 10-11) with TGG (i.e., YGG product). Gottlieb also teach treating AIDS patients (Example 7) with TGG in order to improve their immune system. These methods are encompassed in claims 1-10 and 12-14. Although neither patient is identified as having the metabolic syndrome or symptoms thereof, it would have been obvious to one of ordinary skill in the art to apply YGG to patients of cancer and AIDS which would present at least one metabolic syndrome symptom (such as obesity, high blood pressure, hypercholesterolemia, etc) and having the metabolic syndrome. One of ordinary skill in the art would have been motivated to do so since there are no limitations expressly taught by Gottlieb with regards to the type of patient that would respond to the immune boosting to YGG product. Moreover, the limitations in the preamble “controlling inflammation”, “mitigating a symptom”, “preventing chronic inflammation”, and so forth, necessarily read upon the method of Gottlieb since it teaches the instant steps. The limitations of claim 18 are taught in Examples 6-7, which teach blood tests measuring the patient’s immune system, however, the Examples do not expressly teach monitoring inflammation and glucose level. The adjustment of particular conventional working conditions (e.g., determining types of patients that respond to the treatment, determining appropriate health indicators within such method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of

the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., type of patients [e.g., having obesity, high blood pressure, metabolic syndrome, and so forth) and health parameters to be measured as health indicators], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions including type of patients wherein the method can be effective, in the safest and most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Marcela M Cordero Garcia/
Examiner, Art Unit 1654

MMCG 12/08